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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/316,313	05/21/1999	RAM PRATAP	U-012254-3	7625

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 07/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/316,313	PRATAP ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-18 and 23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18, 23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 11-18, 23-32 are pending. Claim 22 has been canceled according to the amendment filed on 8-19-2004.

Claim Rejections - 35 USC § 103

2. The rejection under 35 U.S.C. 103(a) as being unpatentable over Nodiff (5104885) in view of Paliwal et al. (Journal of Chromatography, 1993, 616:155-160) and Puri et al. (Am. J. Trop. Med. Hyg., 1989, 41(6): 638-642) is replaced by the new 103 rejection set forth in paragraph 3 below.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-18, 23-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nodiff (5104885) in view of Paliwal et al. (Journal of Chromatography, 1993, 616:155-160) and Puri et al. (Am. J. Trop. Med. Hyg., 1989, 41(6): 638-642).

Primaquine is known to be a clinically effective radically curative antimalarial drug with tissue schizonticidal and gametocidal activity (column 2, lines 20-25), thereby inhibiting the transmission of malaria as recited in the instant claims. The inhibition of the transmission of malaria as recited in the instant is therefore an inherent property of primaquine. An increase of the survival time may be achieved by a single dose of the drug compound administered after infection, whereas for radical curative treatment in a mammal, a single dose of the drug compound is administered for 7 days (columns 18-20).

Primaquine has limited use because of its toxicity (column 2, lines 20-30). CDR1 80/53 (the other name for the instant compound according to ACS Registry file) known to be a prodrug of primaquine, has similar anti-malarial activity but has much less toxicity than primaquine (Paliwal, page 155, first paragraph). The properties recited in the instant claims 13-14 are intrinsic to the compound CDR1 80/53.

While Paliwal does not recite the dosage as in the instant, Puri teaches the curative dose for CDR1 80/53 as 1.25 mg/kg per day for 7 days (page 638, *Experimental groups*), which is within the instant 'less than 5 mg/kg of the body weight of the animal for at least 7 day period' as recited in instant claims 24-32.

At the time of the invention, one of ordinary skill in the art would be motivated to replace the toxic primaquine to combat malaria with its less toxic CDR1 80/53 prodrug of Paliwal at the curative dosage, either as a single dose, or daily for 7 days as taught by Puri and Nordiff to arrive at the instant invention.

Claim Rejections - 35 USC § 112(1)

4. In view of the amendment, the rejection for Claims 11-18, 23-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is replaced by the new 112 first paragraph rejection set forth in paragraph 5 below.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15, 23-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The 'less than 1.0 mg/kg of the body weight of the animal per day' as recited in the amended claim 11 is not described in the specification. Applicants submit that it has support in Group 5, Table IV on page 22 of the specification. However, '1.0 mg/kg of compound 1' as recited in Table IV is probably an error, because according to the in the description of the data of Table IV on page 16 of the specification, Group V is the vehicle control group, which 'showed marginal fluctuation of met-Hb level within the normal limits'. Furthermore, it is recited that 1.25 mg/kg is the curative dose for compound I (page 16 of the specification).

The description for 'a single dose that does not exceed 5.0 mg/kg of the body weight of the animal for reducing infectivity for at least a 7 day period' of the amended claim 24 is not found in the specification or in the original claims.

The rejection is applicable to claims dependent on claim 11 or 24.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15, 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. Nature of the invention.

The amended claim is directed to a method for inhibiting transmission of malaria with the compound of formula (1) with an amount less than 1.0 mg/kg of the body weight of the animal per day.

b. State of the prior art and the predictability/unpredictability of the art.

Puri teaches that 1.25 mg/kg is the curative dose for compound I (page 638).

On page 16 of the specification, applicants also recite that the curative dose of compound I is 1.25 mg/kg.

The high degree of unpredictability is well recognized in the pharmaceutical art. For example, while 2 out of 2 monkeys show significant reduction in oocyst number and percent infectivity at the 1.25 mg/kg dosage of compound I, only 2 out of the 3 monkeys show significant reduction in oocyst number and percent infectivity at the 2.5 mg/kg dosage.

c. *Amount of guidance/working examples.*

In Table I on page 18 of the specification, a dose of 0.63 mg/kg only shows some reduction in oocyst number and the percent infectivity. The data are derived from only one monkey. Inhibition of malaria transmission at less than 1.0 mg/kg, such as 0.63mg/kg, therefore cannot be concluded from these data in view of the high degree of unpredictability in the art (paragraph b above).

d. *The breadth of the claims.*

In view of the established curative dose of 1.25 mg/kg and the high degree of unpredictability of the art (paragraphs b, c above), applicants' assertion that 'less than 1.0 mg/kg of the body weight of the animal per day' would inhibit the malaria transmission as recited in the instant claims is not commensurate with the scope of the objective enablement.

e. *Quantitation of undue experimentation.*

Since insufficient teachings and guidance have been provided in the specification (paragraphs b-d above), one of ordinary skill in the art would not be able to use the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 112(2)

7. The rejection for Claims 16-18, 24-30, 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is replaced by the new rejection in paragraph 8 below.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention..

Claims 13, 24-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 24, the meaning of the 'single dose that does not exceed 5.0 mg/kg of the body weight of the animal for reducing infectivity for at least a 7 day period' is unclear. Does it mean a single dose daily for at least 7 days? Or does it mean the animal does not get infected for at least 7 days, but can become infected in day 8 ? or none of the above?

b. Claim 14, it is recommended that 'of the' be inserted after 'enaminone functionality' to better define the claim.

c. Claim 13, the meaning of 'a ***composition*** has a slow metabolic degradation' is unclear since carriers/excipients in the composition are not known to be subjected to metabolic degradation. Does applicant intend the ***compound*** in the composition has a slow metabolic degradation?

The rejection is applicable to claims dependent on the above claims.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625